REMARKS

I. Petition for Extension of Time

Applicants herewith petition the Commissioner for Patents to extend the time for response to the Office Action mailed September 8, 2004 for one month from December 8, 2004 to January 8, 2005. Authorization is given to charge the extension of time fee of $120.00 (37 C.F.R. §§1.136 and 1.17) to Deposit Account No. 23-1703. Any deficiency or overpayment should be charged or credited to the above numbered deposit account.

II. Claim Rejection - 35 U.S.C. §112

Claim 46 is rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. In the Office Action mailed May 23, 2003, the Examiner specifically objected to the recitation of the term "prevention". Claim 46 has been amended by the deletion of the word "preventing" and substitution with -- inhibiting --.

Withdrawal of the §112 rejection is requested.

III. Claim Rejection – 35 U.S.C. §§102/103

Claims 1, 2-4, 19, 23, 25, 27, 29-34 and 39-46 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by WO 88/00829 for the reasons set forth in the Office Action of May 23, 2003.

Claims 5, 10, 11, 15, 16, 20, 22, 24, 26, 28 and 47 are rejected under 35 U.S.C. §103 as allegedly being unpatentable over WO 88/00829 for the reasons set forth in the Office Action of May 23, 2003.

In response to the Office Action of May 23, 2003, Applicants submitted a response on September 22, 2003. In the next Office Action, the §§102/103 rejections based on WO 88/00829 were withdrawn. Instead, the Examiner cited US 5,646,134 to ("Yates"). Applicants addressed

the §§102/103 rejections based on Yates in a response filed May 20, 2004. In the outstanding final Office Action, the Examiner has withdrawn the §§102/103 rejections based on Yates and reverted to WO 88/00829.

It is the Examiner's position that the pharmaceutical composition of the claimed invention is the same as the pharmaceutical composition disclosed by WO 88/00829. It is also the Examiner's position that the route of administration of the claimed and prior art pharmaceutical compositions, i.e., oral vs. nasal, is irrelevant. Applicants respectfully disagree.

The Examiner's attention is directed to M.P.E.P. §2141.02 (2100-120) where the following direction is given:

> **PRIOR ART MUST BE CONSIDERED IN ITS ENTIRETY, INCLUDING DISCLOSURES THAT TEACH AWAY FROM THE CLAIMS**
>
> A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984) (Claims were directed to a process of producing a porous article by expanding shaped, unsintered, highly crystalline poly(tetrafluoroethylene) (PTFE) by stretching said PTFE at a 10% per second rate to more than five times the original length. The prior art teachings with regard to unsintered PTFE indicated the material does not respond to conventional plastics processing, and the material should be stretched slowly. A reference teaching rapid stretching of conventional plastic polypropylene with reduced crystallinity combined with a reference teaching stretching unsintered PTFE would not suggest rapid stretching of highly crystalline PTFE, in light of the disclosures in the art that teach away from the invention, i.e., that the conventional polypropylene should have reduced crystallinity before stretching, and that PTFE should be stretched slowly.).

The cited prior art WO 88/00829 discloses a composition containing a bisphosphonate and absorption enhancer for nasal administration. The publication expressly teaches away from the oral administration of bisphosphonates. Specifically, the following disclosure appears at page 1, lines 13-20 of WO 88/00829:

> Bisphosphonates have hitherto been administered either orally or intravenously to patients. ***However, the oral absorption is poor and often accompanied by gastrointestinal side effects. Furthermore, the degree of absorption shows substantial individual variations.*** Consequently, intravenous administration has up till now had to be used whenever a rapid and reliable delivery of bisphosphonates was needed. (Emphasis added)

As required by M.P.E.P. §2141.02, the Examiner must consider the entirety of the reference including the disclosure by WO 88/00829 of the disadvantages associated with the oral administration of bisphosphonates. In view of prior art disclosure of the disadvantages associated with the oral administration of bisphosphonates, Applicants submit the following:

1. contrary to the Examiner's position, the prior art recognizes differences with respect to the route of administration of bisphosphonates;
2. WO 88/00829 teaches away from the claimed invention, i.e., oral dosage form and oral administration; and
3. the reported increase in the oral bioavailability in the section entitled "Biological evaluations" at pages 10-11 of the specification is an unexpected advantage.

For all of the foregoing reasons, Applicants submit that the Examiner's reliance on WO 88/00829 does not support a *prima facie* case of obviousness. This is especially true in view of the entirety of the reference including the disclosures teaching away from the claimed oral dosage form. Withdrawal of the §§102/103 rejections based on WO 88/00829 is requested.

CONCLUSION

Applicants submit that pending claims 1-21, 23-34, 40-42 and 45-47 are in condition for allowance, which action is earnestly solicited. The Assistant Commissioner is hereby authorized to charge Deposit Account No. 23-1703 in the event that any fee is required in connection with this communication.

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Respectfully submitted,

John M. Genova
Reg. No. 32,224
Attorney for Applicants

Customer No. 007470
Direct Dial: (212) 819-8832